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Perspective

A Mediation Analysis of Malaria Prevention in Pregnancy and its Effects on Infant Growth

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DESCRIPTION

Child growth struggling a significant public health challenge, contributing to an increased burden of disease. It is associated with heightened risks of mortality and infections during childhood, as well as reduced productivity in adulthood. In low-income and middle-income countries, growth faltering often begins before the age of six months, a period prior to the introduction of complementary feeding and most child nutrition interventions. In malaria-endemic regions, prenatal malaria infection may be a critical factor in growth faltering due to its impacts on maternal inflammation, anaemia and intrauterine growth restriction. These effects are linked to adverse pregnancy outcomes such as low birth weight, preterm delivery, stillbirth and fetal death, all of which contribute to poor growth in infancy.

In regions with moderate-to-high transmission of plasmodium falciparum malaria, the World Health Organization (WHO) recommends Intermittent Preventive Treatment during pregnancy (IPTp) with Sulfadoxine-Pyrimethamine (SP). This strategy is aimed at reducing the risk of malaria in pregnancy and its associated complications. However, in parts of Eastern and Southern Africa, the effectiveness of SP has significantly diminished due to increasing parasite resistance. In high-SP-resistance areas, trials conducted in Kenya and Uganda have demonstrated that IPTp with Dihydroartemisinin-Piperaquine (DP), an alternative antimalarial regimen, was more effective at preventing malaria during pregnancy compared to SP. However, these studies did not find a significant improvement in birth outcomes, such as birth weight or gestational age, when using IPTp-DP compared to IPTp-SP. Ideally, IPTp regimens should not only improve birth outcomes but also promote better growth and development in infancy and beyond. Yet, to date, no studies have investigated the impact of IPTp on child growth during the first year of life.

The potential effects of SP and DP on child growth are likely to differ due to their distinct mechanisms of action. DP, with its higher efficacy against malaria, may influence child growth by reducing the risk of maternal malaria and its associated complications, such as placental malaria. Placental malaria is a major contributor to poor birth outcomes and has been linked to impaired height and weight gain during infancy. On the other hand, SP possesses antibiotic properties that may impact maternal health and subsequently, child growth. For example, a previous study found that SP's positive effect on birth weight was mediated by maternal gestational weight gain, which has a strong association with child growth.

Another significant pathway through which malaria and its treatment may affect child growth is maternal inflammation. Malaria infection during pregnancy, particularly the sequestration of Pf parasites in the placenta, can trigger inflammation and disrupt placental function. This can impair nutrient transport to the fetus and hinder foetal development, resulting in low birth weight or stunted growth. Addressing maternal inflammation through effective malaria prevention could therefore have downstream benefits for infant growth during the first year of life.

Given these pathways, it is plausible that IPTp-DP, by reducing the risk of malaria and its associated complications, may have lasting benefits for child growth. Similarly, SP may influence child growth indirectly by improving maternal nutrition and health during pregnancy. However, these hypotheses remain largely unexplored, as previous studies have focused primarily on birth outcomes rather than long-term growth trajectories.

Using data from a randomized controlled trial conducted among Ugandan mother-infant dyads, our study aimed to address this gap by evaluating whether IPTp-DP improves infant growth during the first 12 months of life compared to IPTp-SP. Additionally, we sought to identify potential mediators of the effects of IPTp on child growth. Specifically, we examined the roles of maternal inflammation, anaemia, preterm birth, gestational weight gain and birth weight and length in mediating the relationship between IPTp regimens and child growth outcomes. By investigating these pathways, our study provides valuable insights into the mechanisms through which malaria prevention during pregnancy may influence child growth, offering a basis for optimizing maternal and child health interventions in malaria-endemic settings.

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CONCLUSION

In conclusion, child growth faltering remains a critical public health issue, particularly in malaria-endemic regions, where prenatal malaria infection significantly contributes to poor growth outcomes. Effective malaria prevention strategies during pregnancy, such as IPTp-DP, have the potential to improve maternal and infant health by reducing malaria-related complications, including placental inflammation and intrauterine growth restriction. This study highlights the importance of understanding the distinct pathways through which antimalarial regimens like SP and DP influence child growth during infancy. By addressing maternal health factors, such as inflammation, anaemia and gestational weight gain, targeted interventions can optimize growth trajectories and improve long-term outcomes in malaria-endemic settings.